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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KUBELIK, ANNE R	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 03/12/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/032,717	ABAD ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,9-12,17-19 and 38-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,9-12,17-19,38,41-43 and 46-54* is/are rejected.

7)☒ Claim(s) *39,40,44 and 45* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5,7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election of Group I and SEQ ID NO:1 in Paper No. 9, filed 23 December 2002, is acknowledged. Because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 4-8, 13-16 and 20-37 have been canceled, claims 1, 9 and 17 have been amended and claims 38-54 have been added as requested in Paper No. 9. Claims 1-3, 9-12, 17-19 and 38-54 are pending.

3. Applicant is reminded that when making amendments to the claims, a parenthetical expression should follow the claim number indicating the status of the claim, *e.g.*, "amended," "twice amended," etc. The parenthetical expression should be the same for both the clean version of the claim and the marked up version. See 37 CFR 1.121 and MPEP 714.

4. The abstract is not descriptive of the instant invention, which is nucleic acid encoding a *Bacillus thuringiensis* toxin, expression cassettes comprising the nucleic acid, plants and seeds comprising a construct comprising the nucleic acid and a method of using it to impact a plant pest. A new abstract is required that is clearly indicative of the invention to which the claims are directed. The abstract of the disclosure should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

5. The title of the invention is not descriptive of the instant invention, as above. A new title is required that is clearly indicative of the invention to which the claims are directed. Note that titles can be up to 500 characters long.

6. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However,

this application fails to comply with the requirements of 37 CFR 1.821 through 1.825.

Sequence identifiers are missing from pg 14, line 22, pg 15, line 20, pg 16, line 4, pg 20, lines 18 and 20, pg 21, line 6, pg 26, line 24, pg 27, lines 8 and 16, pg 69, lines 2 and 6, and all other mentions of NGSR, LRMS and LKMS as amino acid sequences. Sequence identifiers are also missing from pg 27, line 15.

Full compliance with the sequence rules is required in response to this Office action. A complete response to this Office action must include both compliance with the sequence rules and a response to the issues set forth below. Failure to fully comply with both of these requirements in the time period set forth in this Office action will be held to be non-responsive.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-3, 9-12, 17-19, 38, 41-43,46-49 and 52-54 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids encoding SEQ ID NO:2 and 10, expression cassettes comprising the nucleic acid, plants and seeds comprising a construct comprising the nucleic acid and a method of using it to impact a plant pest, does not reasonably provide enablement for any nucleic acid that has 90% identity to SEQ ID NO:1, that hybridizes to SEQ ID NO:1 or that is antisense to a nucleic acid with 90% identity to SEQ ID NO:1, expression cassettes comprising the nucleic acid, plants and seeds comprising a construct comprising the nucleic acid and a method of using it to impact a plant pest. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly

connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to a nucleic acid with 90% identity to SEQ ID NO:1 or that hybridizes to SEQ ID NO:1, expression cassettes comprising the nucleic acid, plants and seeds comprising a construct comprising the nucleic acid and a method of using it to impact a plant pest. The claims are also drawn to an antisense version of a nucleic acid with 90% identity to SEQ ID NO:1, plants transformed with it and a method of using it to impact a plant pest.

The instant specification, however, only provides guidance for methods of assaying the activity of *B. thuringiensis* strain 1218 and lysate against Western corn rootworm and Southern corn rootworm (examples 1 and 2); isolation of crystal protein from the strain and assaying of it for pesticidal activity against western corn rootworm (example 3); identification of two coding regions, *Cry1218-1* and *Cry1218-2* (SEQ ID NO:1 and 3, with SEQ ID NOs:27 and 28 as the genomic clones), isolated by unknown methods, as encoding proteins, SEQ ID NOs:2 and 4, respectively, that have homology to Cry8Ba1 (example 4); production of truncated proteins, SEQ ID NOs:16 and 18, encoded by SEQ ID NOs:16 and 18 respectively, in *E. coli* that are active against southern corn rootworm (example 4); and production of maize-preferred coding sequences of a different truncated version of Cry1218-1 - the nucleic acid is SEQ ID NO:9, which encodes SEQ ID NO:10 (example 5). The specification also teaches making mutant versions of truncated Cry1218-1 (SEQ ID NO:16), one of which has a truncated N-terminus (amino acids 43-663 of SEQ ID NO:16), and the other in which NGSR has been inserted after amino acid 164 - all of these mutant proteins are effective against Colorado potato beetle (example 6) and other mutant proteins (SEQ ID NOs:32,34, 42 and 46) that have added chymotrypsin cleavage sites - all are more effective against southern and western corn rootworm than Cry1218-1 (example 7). The specification also teaches transformation of maize with SEQ

ID NO:9 (examples 8 and 9).

The instant specification fails to provide guidance for any nucleic acid with 90% identity to SEQ ID NO:1 or that hybridizes to SEQ ID NO:1, expression cassettes comprising the nucleic acid, plants and seeds comprising a construct comprising the nucleic acid and a method of using it to impact a plant pest. SEQ ID NO:3 is 92.1%, not 90%, identical to SEQ ID NO:1 (see sequence search results). For example, the specification fails to provide guidance for the exact hybridization or amplification conditions and probes/primers to use in isolation of nucleic acids other than SEQ ID NOs:1 and 3.

The specification teaches making mutant versions of truncated Cry1218-1, but as only a few amino acids were modified and at only one site in the protein, producing nucleic acids with about 99.4% identity to SEQ ID NO:1. No nucleic acids were made that have 90% identity to SEQ ID NO:1.

The specification on pg 28, lines 5-11, suggests making these nucleic acids by making conservative substitutions in the encoded protein. However, making "conservative" substitutions (*e.g.*, substituting one polar amino acid for another, or one acidic one for another) does not produce predictable results. Lazar et al (1988, Mol. Cell. Biol. 8:1247-1252) showed that the "conservative" substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while "nonconservative" substitutions with alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach that when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically reduced enzyme activity (see

Table 1). All these mutated proteins, however, would have at least 95% identity to the original protein. The nucleic acids encoding all these mutated proteins, however, would hybridize under high stringency to the nucleic acids encoding the original protein.

Furthermore, claims 41, 47 and 53 are drawn to an antisense version of a nucleic acid with 90% identity to SEQ ID NO:1, plants transformed with it and a method of using it to impact a plant pest. When a plant is transformed with a sense version of a Bt toxin, the toxin is expressed, and the toxin itself, a protein, acts against the plant pest. When a plant is transformed with an antisense version of gene, the antisense RNA acts against either an endogenous RNA to inhibit its expression or acts against RNA produced by an invading pathogen to inhibit expression of one or more of its genes. As neither the plant nor the plant pest natively expresses Bt toxin, and as expression of Bt toxin is required for controlling plant pests, expression of an antisense version of the Bt-toxin encoding SEQ ID NO:1 cannot control plant pests. The specification does not teach a method for using antisense molecules to a Bt-toxin gene to make pest resistant plants.

Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate nucleic acids with 90% identity to SEQ ID NO:1 or that hybridizes to SEQ ID NO:1. Making all possible single amino acid substitutions, which would involve making 1-3 nucleotide substitutions, in an 1206 amino acid long protein like that encoded by SEQ ID NO:1 would require making and analyzing 19^{1206} nucleic acids; these nucleic acids would have about 99.9% identity to SEQ ID NO:1. Because nucleic acids that have 90% identity to SEQ ID NO:1 or that hybridize to SEQ ID NO:1 would encode proteins with 120 amino acid or more substitutions, many more than 19^{1206} nucleic acids would need to be made and analyzed.

As the specification does not describe the transformation of any plant with any nucleic acid with 90% identity to SEQ ID NO:1 or that hybridizes to SEQ ID NO:1, undue trial and error experimentation would be required to screen through the myriad of nucleic acids encompassed by the claims and plants transformed therewith, to identify those that could control plant pests, if such plants are even obtainable.

Given the claim breath, unpredictability in the art, undue experimentation, and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

9. Claims 1-3, 9-12, 17-19, 38, 41-43,46-49 and 52-54 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a multitude of nucleic acids that have 90% identity to SEQ ID NO:1 or that hybridize to SEQ ID NO:1, expression cassettes comprising the nucleic acids, plants and seeds comprising constructs comprising the nucleic acids and a method of using them to impact a plant pest. In contrast, the specification only describes a coding sequence from *B. thuringiensis* strain 1218 that comprises SEQ ID NO:1. Applicant does not describe other DNA molecules encompassed by the claims, and the structural features that distinguish all such nucleic acids from other nucleic acids are not provided.

Additionally, the function of the protein encoded by the claimed nucleic acid is not recited in claims 1-3, 38, 41-42, 47-48 and 53-54.

Hence, Applicant has not, in fact, described nucleic acids within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed

invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

See *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997):

> The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA .... Accordingly, the specification does not provide a written description of the invention ....

and at pg 1406:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 17-19, 41-42 and 47-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

Claims 41, 47 and 53 are indefinite in their recitation of "An antisense nucleotide

sequence corresponding to the nucleotide sequence of claim 1". It is not clear if the antisense sequence comprises all of the nucleic acid of claim 1, if it is a nucleotide sequence that is antisense to only a portion of the nucleic acid, or if it "corresponds" in some other manner. Thus, the metes and bounds of the claimed nucleotide sequence are unclear.

Claims 42, 48 and 54 are indefinite in their recitation of "stringent conditions". It is not clear what hybridization and wash conditions are considered stringent. Thus, the metes and bounds of the claimed nucleotide sequence are unclear.

Claims 17-19 and 49-54 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The method is one of impacting a plant pest. The only step is one of transforming a plant or cell with a nucleic acid. The omitted steps are those in which the plant pest is impacted. It is suggested that the claims be amended to indicate that the resulting transformed plant or cell impacts the plant pest.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 42, 48 and 54 are rejected under 35 U.S.C. 102(b) as being anticipated by Michaels et al (1996, US Patent 5,554,534).

Michaels et al teach an nucleic acid that would hybridize to SEQ ID NO:1 under "stringent conditions" because it has 85.1 identity to SEQ ID NO:1 (see sequence search results).

Michaels et al also teach plants transformed with constructs comprising the nucleic acid and a method of using it to impact a plant pest (column 15, line 5, to column 16, line 35).

14. Claims 1-3, 9-12, 17-19, 38-41, 43-47 and 49-53 are free of the prior art, given the failure of the prior art to teach or suggest an isolated nucleic acid that has at least 90% identity to SEQ ID NO:1 or antisense molecules to that nucleic acid.

15. Claims 50-51 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

16. Claims 39-40 and 44-45 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (703) 308-0198.

Anne R. Kubelik, Ph.D.
March 6, 2003